REMARKS

Claims 1 and 15-33 are pending in the present application. Claims 1, 15-19, 22-24, and 28-32 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 7,284,668 (Charkoudian). Claims 20-21, 32 and 33 are rejected under 35 U.S.C. §103(a) as being unpatentable over Charkoudian in view of U.S. Patent No. 7,108,791 (Tkacik). Claims 1 and 15-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 7,140,496 (Nagoya). By this amendment, claim 1 has been amended. Support for this amendment can be found, for example, in the specification on page 16, lines 8-18; page 41, lines 26-28; page 42, lines 16-26; and page 43, lines 7-21. Therefore, no new matter has been added. Reconsideration of the present application is respectfully request in light of the amendments above and remarks below.

Initially, Applicants respectfully request acknowledgment of the information disclosure statements file on April 18, 2005 and July 25, 2005.

Claims 1, 15-19, 22-24, and 28-32 are rejected under 35 U.S.C. §103(a) as being unpatentable over Charkoudian. Applicants respectfully traverse this rejection.

Among the limitations of independent claim 1 not taught or suggested by Charkoudian is a "hydrophilic microporous membrane ... having been contacted with a hydrophilic vinyl monomer having one vinyl group after generation of radicals by irradiation with ionizing radiation in order to be subjected to hydrophilizing treatment by a graft polymerization reaction, and having a maximum pore size of 10 to 100 nm, wherein said hydrophilic microporous membrane has a coarse structure layer with a higher open pore ratio and a fine structure layer with a lower open pore ratio which are formed in one piece."

Also among the limitations of independent claim 1 not taught or suggested by Charkoudian is "said coarse structure layer exists on at least one side of the membrane

surface and has a thickness of 2 μm or more and a thickness of said fine structure layer is 50% or more of the whole membrane thickness"

Charkoudian discloses a porous media or membranes having a surface coating that includes a first coating of a cross-linked terpolymer and a second coating of a copolymer or a terpolymer modified with a hydrophilic or hydrophobic functional group. *See* Charkoudian, Abstract. The Examples in Charkoudian disclose that the porous membrane can be modified with a second coating which provides, for example, a positively charged surface, a negatively charged membrane, a reactive nucleophilic affinity functionality, a reactive electrophilic affinity functionality, or a superphobic surface. *See* Charkoudian, Examples 1-5.

In contrast to Charkoudian, the present claims explicitly recite that the membrane "has a coarse structure layer with a higher open pore ratio and a fine structure layer with a lower open pore ratio which are formed in one piece, and said coarse structure layer exists on at least one side of the membrane surface and has a thickness of 2 μm or more and a thickness of said fine structure layer is 50% or more of the whole membrane thickness." As a result of the recited structure, a hydrophilic microporous membrane has the ability to remove small viruses such as parvovirus and allows permeation of physiologicaly active high-molecular-weight substances, such as globulin and Factor VIII, at a high rate and in large quantities. *See e.g.* specification, p. 5, ll. 5-15. The coarse structure layer of the recited structure, alleviates the decrease in filtration rate due to the blockage by impurities and can be used without reducing removing performance, such as for viruses. See e.g. specification, p. 17, ll. 6 -8, 16-19).

Also in contrast to Charkoudian, the present claims recite that the membrane is subjected to hydrophilizing treatment by a graft polymerization reaction and has a maximum pore size of 10 to 100 nm. The recited structure hydrophilizes the microporous membrane and reduces the adsoptivity of protein. In a graft polymerization reaction, the

microporous membrane is contacted with a hydrophilic vinyl monomer which has one vinyl group after generation of radicals by irradiation with ionizing radiation.

The graft polymerization method by irradiation with ionizing radiation is roughly divided into (1) a pre-irradiation method in which radicals are generated in the membrane and subsequently the membrane is contacted to the reactant compounds; and (2) a simultaneous irradiation method in which radicals are generated in the membrane while the membrane is contacted to the reactant compounds. Oligomers can be more frequently generated by the simultaneous irradiation method. Since it is difficult to sufficiently wash out and remove the oligomers, especially from the small-pore-size membrane having a maximum pore size of 10 to 100 nm such as the present invention, the present claims recite the application of the pre-irradiation method.

The present invention is different from Charkoudian, which discloses that the formation of a first and a second surface on the membrane substrate in patent '668 includes some steps such as: (d) contacting the surface of said porous membrane substrate with a reactant solution containing a specific monomer; (e) removing the membrane substrate from the solution; (f) polymerizing said monomers to form said heat stable biomolecule resistant surface; (g) washing said membrane to form the first coating on the porous substrate; and (h) contactng the membrane from step (g) with an aqueous solution of the monomers, a cross-linking agent and a photo initiator; (i) removing the porous membranes in step (h) from the aqueous solution; and (j) exposing the membrane from step (i) to ultraviolet light (for cross-linking polymerization). *See* Charkoudian, col. 6, l. 21 – col. 7, l. 8.

The above-mentioned steps in Charkoudian include a polymerization step under a condition where a membrane contacts with a monomer. As a result, Charkoudian has the major disadvantage of producing a large amount of oligomers. A large amount of oligomers are not removed by a washing operation and left in the small-pore-size membrane.

Charkoudian fails to teach or suggest all the limitations of independent claim 1. Accordingly it is respectfully submitted that claim 1 patentable distinguishes over Charkoudian.

Claims 15-19, 22-24, and 28-32 depend directly or indirectly from and contain all the limitations of independent claim 1. Each of these dependent claims recite additional limitations, which in combination with the limitations of claim 1, are neither taught nor suggested by the prior art of record. Accordingly, claims 5-19, 22-24, and 28-32 are likewise patentable.

Claims 20-21, 32 and 33 are rejected under 35 U.S.C. §103(a) as being unpatentable over Charkoudian as applied to claims 1, 15-19, 22-24, 28-31 above, and further in view of Tkacik.

As discussed above, Charkoudian fails to teach or suggest all the limitations of independent claim 1. Claims 20, 21 and 32 depend directly or indirectly from and contain all the limitations of independent claim 1. Each of these dependent claims recite additional limitations, which in combination with the limitations of claim 1, are neither taught nor suggested by the prior art of record. Tkacik was cited for additional limitations, none of which cure the deficiencies in Charkoudian. Accordingly, claims 5-19, 22-24, and 28-32 are likewise patentable.

Among the limitations of independent claim 33 not taught or suggested in the cited references is a membrane with "a logarithmic reduction value of porcine parvovirus" under the recited conditions.

Tkacik discloses a method for removing a virus and a filtration capsule used for the method. The efficiency for removing virus (LRV) is improved by using asymmetric ultrafiltration membranes in piles. *See e.g.* Tkacik, Abstract, Fig. 3. Although Tkacik discloses prior art relating to asymetric membranes and a method for hydrophilization, it

does not disclose any features of the hydrophilic microporous membrane of the presently recited invention. *See e.g.* Tkacik, col. 10, ll. 3 -49.

In Tkacik, the performance of the membrane for removing bacteriophage FX174, which is a model small virus, is evaluated. See Tkacik, Example 4; Fig. 3. According to Fig. 3 of Tkacik, the LRV of one layer membrane (corresponding to a single filtration) is less than three when filtration volume is 50. Therefore, the efficiency for removing a small virus is insufficient.

On the other hand, the claim 33 explicitly recites that the LRV for porcine parvovirus of the hydrophilic microporous membrane of the present invention is "3 or more," even when 50 to 55 (L/m^2) is filtrated with a single filtration.

In addition, porcine parvovirus, which is the model virus used in the present invention, is smaller than bacteriophage FX174, which is a model virus used in Tkacik. Therefore, Tkacik does not show a sufficient performance for removing porcine parvovirus, which is smaller than bacteriophage FX174 disclosed in Example 4 of Tkacik.

Charkoudian fails to teach or suggest all the limitations of independent claim 33. Accordingly it is respectfully submitted that claim 33 patentable distinguishes over Charkoudian.

Claims 1 and 15-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of Nagoya. In response to the nonstatutory obviousness-type double patenting rejection, Applicants submit herewith a terminal disclaimer, disclaiming the term of the present application to Nagoya.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: July 18, 2008

Respectfully submitted,

By_____
Charles E. Miller
Registration No.: 24,576
DICKSTEIN SHAPIRO LLP
1177 Avenue of the Americas
New York, New York 10036-2714
(212) 277-6500
Attorney for Applicant